REMARKS

The applicants thank the Examiner for the thorough consideration given to the present application. By the foregoing amendments, discussed below, the applicants attempt to address the various grounds of rejection in the Office Action.

DRAWINGS

Enclosed herewith are four black and white photographs which are submitted under 37 CFR 1.84(b) and M.P.E.P. § 608.02 to serve as formal drawings in lieu of India ink drawings. Due to the nature of the drawings, it is not practical to illustrate the subject matter of the photographs in ink drawings.

In the Office Action, the Examiner made reference to the need for filing a petition under Rule 84. The applicants assume that the Examiner's comment was made in the event that the applicants filed color photographs. In the case of black and white photographs, M.P.E.P. § 608.02 (the relevant portion of which is attached) provides:

> BLACK AND WHITE PHOTOGRAPHS
>
> Photographs submitted in lieu of ink drawings must comply with 37 CFR 1.84(b). There is no requirement for a petition or petition fee, and only one set of photographs is required.

The applicants respectfully request that the enclosed photographs be accepted in lieu of ink drawings.

FORMAL OBJECTIONS/REJECTIONS

The specification has been amended to include a brief description of the drawings as well as insert the section headings specified in Rule 77.

By the foregoing amendments, claims 1, 20, 26, 29, 35, 40, 43, 48 and 53 have been amended to overcome the rejections under 35 U.S.C. § 112 set forth in the Office Action. Minor changes have been made to other claims as well, e.g., converting the British spellings.

In particular, claim 1 has been amended to recite a composition which is suitable for injection without requiring a syringe or trocar, namely to recite a composition "having the shape of a needle capable of penetrating cutis or mucosa," as disclosed on page 9, lines 1-2. Claim 1 has also been amended to recite that the composition is injectable without prior dissolution or other reconstitution, as suggested by the Examiner. In addition, claim 1 has been amended to recite a lower limit (25% by weight of the composition) for the therapeutic agent, discussed further below.

Claim 20 has been amended to delete the phrase, "a derivative thereof," and claim 26 has been amended to replace the term "sugar alcohols" with "sugar alcohol," in order to overcome the indefiniteness rejections. Claims 29 and 48 have been amended to replace the phrase, "the temperature interval," with "a temperature interval," in order to provide a proper antecedent basis. Claim 35 has been amended to delete the phrase, "preferably being a protein selected from insulin, glucagon,

growth hormone, growth factor such as FVII and FVIII, GLP-1, EPO, TPO, interferon or derivatives of these proteins," to clarify the scope of the claim.

Claim 40 has been amended to define "Tg" and the word "and" has been added preceding the final step of the claim. Claim 40 also now recites the same lower limit of the therapeutic agent as recited in claim 1.

Claim 43 has been amended so that "preferentially by freeze drying" is deleted to overcome the rejection based on indefiniteness. And, claim 53 has been amended to delete "including man." Claim 59 has been added reciting the deleted part of claim 53.

The non-elected claims (56-58) have been canceled, in light of the restriction requirement being made final.

Claim 35 was rejected as indefinite because the term "stability" does not specify what kind of stability is meant. In the specification (page 14, lines 1-5), one example of stability, namely chemical stability, is mentioned. However, the scope of the claim is intended to include any kind of beneficial stability that a person with ordinary skill in the art would understand relating to a therapeutic agent. For such reasons, the applicants respectfully request reconsideration of the rejection based on indefiniteness.

In light of the foregoing amendments, the applicants respectfully request withdrawal of the objection to the specification and Section 112 rejections of claims 1-14 and 16-55.

PRIOR ART REJECTION

In the last Office Action, claim 52 was rejected under 35 U.S.C. § 102(b) as being anticipated by PCT application WO 96/03978 ("Roser et al."). Claims 1-55 were rejected under 35 U.S.C. § 103(a) as being obvious over Roser et al. The applicants respectfully request reconsideration of such rejections in view of the amendments to the claims.

Claims 1-35 as amended recite a solid pharmaceutical composition in the shape of a needle capable of penetrating cutis or mucosa. Claims 52-54 and 59 recite a method of injecting the needle-shaped composition recited in claim 1. And, claims 40-51 recite a method of preparing a composition for parenteral injection that includes shaping the composition to a predetermined needle geometry.

The claimed composition and method use a binder which constitutes at least 0.5% by weight of the composition, and at least one therapeutic agent that constitutes at least 25% by weight of the composition (meaning that the binder cannot exceed 75% of the composition).

Roser et al. describes a pharmaceutical composition of a glassy matrix comprising a guest substance that may be a drug. The composition may be in a variety of forms, such as needles, powders of microneedles, or microfibers. In the case of powders used for inhalation, the examples in Roser et al. disclose powders which contain up to 20% of the guest substance, meaning that the matrix constitutes at least 80% of the composition. Other than in the powder examples, Roser et al.

does not mention any amount of active substance relative to the amount of glassy matrix.

Roser et al. discloses that the composition can be in the form of needles which can be implanted. However, as noted above, Roser et al. makes no mention of the ratio of guest substance to matrix in such needles. Thus, there is no suggestion in Roser et al. that needles would have a percentage of guest substance which is any greater than the percentage disclosed for powder, i.e., greater than 20%.

Amended independent claims 1, 40, and 52 recite a pharmaceutical composition, or a method of using a pharmaceutical composition, having the shape of a needle capable of penetrating cutis or mucosa where the composition contains at least 25% by weight one or more therapeutic agent. The high content of the therapeutic agent(s) in the claimed composition helps keep the volume of the composition constant. Moreover, by providing a high ratio of therapeutic agent to binder, the size of the needles may be smaller, thereby making injections less painful.

Roser et al. does not disclose or suggest a composition in which the binder is less than 75%, i.e., in which the therapeutic agent is at least 25%. Although Roser et al. mentions that a small delivery system size, preferably coupled with high momentum delivery, would increase the comfort of administration and minimize tissue damage, it does not disclose or suggest making a small delivery system with a high loading content of the active agent. Moreover, Roser et al. describes that larger needles are implanted. It is not obvious for a person of ordinary skill in the art to

create a solid injection composition system with at least 25% therapeutic agent(s) based on the teaching of Roser et al.

The Examiner noted that all of the ingredients as claimed by the present invention are suggested by Roser et al. and it would be obvious for a person of ordinary skill in the art to include them. However, Roser et al. makes no suggestion of using a predetermined binder loading range to reduce the size of the composition delivery system. The solid composition system of the present invention has properties that are not displaced by systems of high binder content disclosed in the examples of Roser et al. There is no suggestion in Roser et al. to use a solid composition system with at least 25% of guest substance. For such reason, a composition system having at least 25% of therapeutic agent is not obvious.

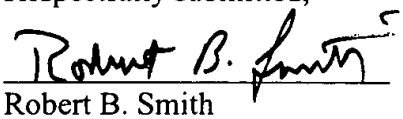
For the foregoing reasons, the applicants respectfully submit that independent claims 1, 40, and 52 are not suggested by Roser et al. The applicants thus respectfully request favorable consideration and allowance of claims 1, 40, and 52, together with the claims dependent thereon.

Original claim 52 was rejected on alternative grounds as anticipated by Roser et al. As amended, claim 52 now recites a method employing the needle shaped composition of claim 1. Because Roser et al. does not disclose or suggest the composition of claim 1, it also does not suggest the step of injecting such a composition as recited in claim 52.

For the foregoing reasons, the applicants respectfully request reconsideration

and withdrawal of the rejection over Roser et al. It is believed that a full and complete response has been made to the outstanding office action, and as such, the present application is in condition for allowance.

Respectfully submitted,



Robert B. Smith
PTO Registration No. 28,538
Attorney for applicant(s)
(212) 735-3020

Skadden, Arps, Slate, Meagher & Flom
Four Times Square
New York, NY 20036-6522

MARKED UP COPY TO SHOW CHANGES MADE

CHANGES TO SPECIFICATION

page 1, line 8:

[Prior art] BACKGROUND OF THE INVENTION

page 4, line 26:

[Summary of the invention] SUMMARY OF THE INVENTION

page 6, line 1:

[Detailed description] DETAILED DESCRIPTION OF THE INVENTION

page 26, line 1:

[Claims] CLAIMS

CHANGES TO CLAIMS

1. (Amended) A solid pharmaceutical composition for parenteral injection, said composition having the shape of a needle capable of penetrating cutis or mucosa, comprising a binder and at least one therapeutic agent, said binder constituting at least 0.5% by weight of the composition and said binder comprising at least one binding agent being a carbohydrate, and said therapeutic agent comprises at least

25% by weight of the composition and said composition comprising [optionally] at least one non-crystallisation agent, whereby said binder forms an amorphous matrix, and whereby such composition is injectable without dissolution or other reconstitution [the amount of said therapeutic agent consisting at least one dosage].

6. (Amended) The composition according to claim 1, wherein [at least 95 % of the strength of the composition is maintained after] the binder essentially remains an amorphous matrix for at least 6 months at ambient temperature.

20. (Amended) The composition according to claim 1, wherein the at least one binding agent being a carbohydrate is a mono-, di-, or oligosaccharide or a corresponding sugar alcohol [or a derivative thereof].

26. (Amended) The composition according to claim 1, wherein the binding agent is maltitol and the non-crystallization [non-crystallisation] agent is sorbitol[,] and/or sugar alcohol[s] of maltotriose and higher oligosaccharides.

29. (Amended) The composition according to claim 1, wherein the viscosity of the composition is less than 50,000 Pa*s in a sub-range of a [the] temperature interval between 60 and 140°C.

35. (Amended) The composition according to claim 1, wherein the therapeutic agent is selected from hormones, antidiabetic drugs, growth factors, and blood factors [, preferably being a protein selected from insulin, glucagon, growth hormone, growth factor such as FVII and FVIII, GLP-1, EPO, TPO, interferon or derivatives of these proteins].

40. (Amended) A method for preparing a solid pharmaceutical composition for parenteral injection comprising mixing at least one therapeutic agent homogeneously with a binder, obtaining an amorphous melt matrix, [whereby] wherein the binder comprises at least one binding agent being a carbohydrate and [optionally] at least one non-crystallisation agent, said binder constituting at least 0.5% by weight of the composition and at most 75% by weight of the composition, and said therapeutic agent comprising at least 25% by weight of the composition, shaping the melt to a predetermined needle geometry, cooling to below the Tg (glass transition temperature) of the binder obtaining the composition, and [optionally] removing the composition from [the mould] a mold cavity.

41. (Amended) The method according to claim 40, [whereby] wherein the melt is injected into a mould cavity having a predetermined geometry.

42. (Amended) The method according to claim 40, [optionally] further comprising a heating step to obtain the amorphous matrix prior to mixing the composition.

43. (Amended) The method according to claim 40, [whereby] wherein prior to melting the binder is dissolved in a solvent, dried, [preferentially by freeze drying,] obtaining a solid amorphous matrix, and [optionally] disintegrating the binder into a powder.

44. (Amended) The method according to claim 40, [whereby] wherein the binder and the at least one therapeutic agent are mixed homogeneously as powders

and melted to form the melt afterwards.

45. (Amended) The method according to claim 43, [whereby] wherein the solvent is water.

46. (Amended) The method according to claim 40, [whereby] wherein the water content of the composition is less than 20% by weight.

47. (Amended) The method according to claim 40, [whereby] wherein the Tg of the binder is at least 30°C.

48. (Amended) The method according to claim 40, [whereby] wherein the viscosity of the composition is less than 50,000 Pa*s in a sub-range of a [the] temperature interval between 60 and 140°C.

49. (Amended) The method according to claim 40, [whereby] wherein the steps of the method are carried out essentially aseptically.

50. (Amended) The method according to claim 40, [whereby] wherein the composition is [moulded] moulded as the second part in a two component [moulding] moulding machine.

51. (Amended) The method according to claim 50, [whereby] wherein a cartridge constituting the [mould] mold cavity is [moulded] molded as the first part in a two component [moulding] molding machine.

52. (Amended) The method of injecting [a] the solid pharmaceutical composition recited in claim 1 through an epidermis or mucosa of an animal comprising arranging a device comprising the solid composition adjacent the epidermis or

mucosa and ejecting the solid composition.

53. (Amended) The method according to claim 52, [whereby] wherein the animal is selected from the group of fish, birds, molluscs, reptiles or mammals [including man].

54. (Amended) The method according to claim 52, [whereby] wherein the composition is injected at least once a day.